IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application Of	: Group Art Unit: 1615
PANKAJ MODI	: Examiner: T. Ware
Serial No. 09/538,829	: Attorney Docket No. 358594-00010-2
Filed: March 30, 2000	:

Entitled:
METHOD FOR ADMINISTERING INSULIN TO THE BUCCAL REGION

APPEAL BRIEF

March 11, 2002

Assistant Commissioner for Patents
BOX AF
Washington, D.C. 20231

Sir:

Appellant respectfully appeals the final rejection issued in the above captioned case on July 12, 2001 and maintained in the Advisory Action issued on December 4, 2001.

Real Party In Interest

The Real Party In Interest is Generex Pharmaceuticals, Inc.. Inventor Pankaj Modi assigned all of his right, title and interest in the invention to Generex Pharmaceuticals, Inc. in an assignment dated January 30, 2002. The document has been filed, but not yet recorded, in the United States Patent and Trademark Office.

Related Appeals and Interferences

There are no related appeals or interferences known to Appellant, Appellant's legal representative or Assignee which will directly affect or be directly affected by or having a bearing on the Board's decision in the pending appeal.

Status of Claims

Claims 26-34 and 36-37 are pending and appealed. Claims 26-27 and 37 have been rejected under 35 USC § 102(e) as being anticipated by Manning et al. (5,770,559). Claims 26-27, 29 and 37 have been rejected under 35 USC § 103(a) as being unpatentable over Manning and as unpatentable over Radhakrishnan (5,049,389). A true and correct copy of all pending claims is attached as Appendix A.

Status of Amendments

The claims were finally rejected in an Office Action mailed July 12, 2001. A response to this action and the Declaration of Pankaj Modi were filed on November 12, 2001. The remarks made in the response were considered by the Examiner and deemed not persuasive. No amendments were submitted with the response.

Summary of Invention

The present invention is generally directed to a method of administering insulin to the buccal region of the oral cavity. The insulin is administered using a metered dose device, and is sprayed into the buccal cavity, while the patient resists inhalation. The insulin is then absorbed through the buccal mucosa to enter the bloodstream, where it can take effect. The invention is further directed to a pharmaceutical composition comprising the insulin, the composition comprising a mixed micelle formulation of various ingredients. Administration of insulin to the buccal region is a significant distinction over the art.

Issues

The issues presented on appeal are 1) whether Claims 26-27 and 37 are properly rejected under 35 USC § 102(e) as being anticipated by Manning, and 2) whether Claims 26-27, 29 and 37 are properly rejected under 35 USC § 103(a) as being unpatentable over Manning and unpatentable over Radhakrishnan.

Grouping of Claims

Claims 26-34 and 36-37 stand or fall together.

Argument

Rejections Under 35 U.S.C. § 102

Claims 26-27 and 37 have been rejected under 35 U.S.C. § 102(e) as being anticipated by Manning et al. (5,770,559). Appellant respectfully submits that Manning does not teach all elements of the claimed invention.

According to the Examiner's statements in the Office Action dated July 12, 2001, inhalation of insulin depends upon the patient and the Appellant has not shown that the patients of the '559 patent do not resist inhalation. The Examiner further asserts that the reference meets the limitations of the present claims because the method of the present claims and the process of administration of an effective dose of insulin in the '559 patent both involve oral administration of insulin.

As previously set forth in Appellant's response, the '559 patent discloses delivery of insulin to the lungs, not delivery of a formulation to the buccal cavity. As established in the Declaration of Pankaj Modi, submitted with the Response of November 12, 2001 (and also attached herewith at Tab B), a method which describes delivery of a formulation to the lungs cannot also be a method in which inhalation is resisted. On the contrary, a formulation that delivers a drug to the lungs requires that a patient inhale the formulation. The '559 patent can be said to "teach away" from resisting inhalation, as it requires the opposite action to provide an effective dose of the composition described in that patent.

Also as established in the Declaration, the method disclosed in the '559 patent, and supported by data therein, simply cannot result in delivery of an effective amount of insulin to the buccal region of oral cavity, as does the method of the present invention. The '559 patent discloses that over 80% of the formulation is delivered to the lungs; any remaining amount (which is not residing in the device itself) is not enough to provide an effective dose of insulin. As described in the Declaration, due to the nature of the drug and the illness being treated, insulin delivery requires a known and precise dosage. The method of administration

described in the '559 patent cannot provide this, and cannot provide an effective amount, as would be understood by one skilled in the art. Therefore, Claims 26, 27 and 37 are not anticipated by the '559 reference.

The Advisory Action states that the claims remain rejected because the instant method does not exclude administration to the lungs, and because the Appellant has not demonstrated that the methods of the prior art do not result in buccal administration. This statement indicates that the Examiner completely disregards the language of the Claim 26, from which 27 and 37 depend, in two respects.

First, Claim 26 specifically recites that insulin is administered to the buccal region "*while resisting substantial inhalation*". As stated above, a method which requires inhalation cannot also be a method in which inhalation is resisted; Manning does not teach or suggest this aspect of the invention, either explicitly or inherently, as asserted by the Examiner, as these methods are mutually exclusive.

Secondly, the Examiner ignores the language "*an effective amount*" as it is found in Claim 26. Manning does not teach or suggest delivery of an effective amount of insulin to the buccal region, nor would the method of Manning inherently result in delivery of an effective amount to the buccal region. The disclosure of Manning speaks for itself, as it describes a method in which *over 80%* of the drug is delivered to the lungs.

To establish anticipation under 35 U.S.C. § 102, every element of a claim must be present in a single reference. (See, for example, *Jamesbury Corporation v. Litton Industrial Products, Inc.*, 225 USPQ 253 (Fed. Cir. 1985), a copy of which is attached at Tab C.) Not every element of Claims 26, 27 and 37 is taught by Manning; Manning does not teach buccal administration while resisting inhalation, nor does Manning teach delivery of an effective amount of a drug to the buccal region. Appellant submits that, as not every element is taught in this reference, the reference is not appropriately cited under §102(b).

Appellant respectfully submits that the inherency argument, on which the Examiner relies, in not supported in the law. According to the MPEP at 2112,

"the fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic", *In re Rejckaert*, 9 F.3d 1531, 1534 (Fed. Cir. 1993) (attached at Tab D). The MPEP goes on to state, "To establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is *necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill* (emphasis added). The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (attached at Tab E). The Examiner has not pointed to any evidence whatsoever indicating that the method of Manning necessarily results in delivery of an effective amount, and that it would be so recognized by one skilled in the art. As stated above, one skilled in the art would not look to a disclosure on lung delivery for guidance on buccal administration. For all of these reasons, Appellant submits that all claims rejected on this basis are allowable.

Rejections Under 35 U.S.C. § 103

Claims 26-27, 29 and 37 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Manning, '559, and allegedly unpatentable over Radhakrishnan (5,049, 389). Appellant respectfully submits that the claims are not obvious in view of either reference

According to the Examiner, both the '559 and '389 patents teach pulmonary administration of the disclosed compositions, which would inherently result in buccal administration. Again, the Examiner disregards the claim language to arrive at this rejection.

As described above, the '559 patent does not teach or suggest delivery of an effective amount of insulin, either explicitly or inherently, nor does it teach administration to the buccal cavity, while resisting inhalation. All arguments made above by Appellant are equally applicable to the §103 basis of rejection as it pertains to this reference; Appellant will not reiterate the entirety of the argument here. The '559 patent provides no guidance whatsoever on buccal delivery of insulin, nor would one skilled in the art look to a disclosure on pulmonary

administration for information on how to deliver a drug by the methods of the present invention.

A reasonable expectation of success must be found in the prior art references to support a rejection under 35 U.S.C. § 103. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) (attached at Tab F). Such an expectation of success has not been demonstrated in the present case. The Examiner has not pointed to any evidence in the reference (as there is none) or elsewhere, which would indicate that one skilled in the art could expect to use the method of that invention to successfully deliver an effective amount of insulin to the buccal region while resisting inhalation, as claimed in the present invention. Appellant submits that the Manning reference does not render Claims 26, 27, 29 and 37 obvious and is not properly cited as a §103 reference.

The '389 patent is also cited for teaching pulmonary administration, which, according to the Examiner, would inherently result in buccal administration. The inherency argument must fail, as demonstrated in the above discussion; all arguments presented above are equally applicable to this reference. Appellant respectfully submits that the present invention is patentable over the '389 patent. The Declaration establishes that the '389 patent does not teach resisting inhalation, and it does not teach delivery of an effective amount of insulin to the buccal cavity, explicitly or inherently. The '389 patent also speaks for itself; Table 9 of that patent discloses that the majority of the composition, an amount *over 80%*, is delivered to the deep lung region.

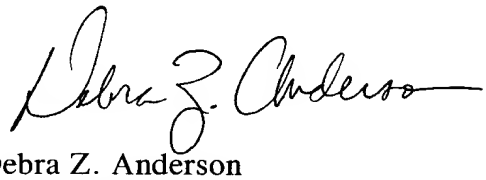
As with the Manning reference, the Examiner cannot point to any evidence whatsoever that would lead one skilled in the art to conclude that the method of Radhakrishnan would result in successful administration of an effective amount of insulin to the buccal region, while resisting inhalation. For all of the above reasons, Appellant submits that all claims rejected on this basis are allowable.

SUMMARY

Appellant respectfully submits that none of the references relied on anticipate or suggest the methods of the present invention. It is respectfully

requested, therefore, that the rejection of the pending claims, Claims 26-34 and 36-37, be reversed, and the case remanded to the Examiner for issue of a Notice of Allowance. Such action is respectfully requested at an early date.

Respectfully submitted,



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In the Claims:

26. A method for administering insulin to the buccal mucosa comprising spraying an effective amount of said insulin to the buccal mucosa using a metered dose inhaler, while resisting substantial inhalation of said insulin.

27. The method of Claim 26, wherein said insulin is in a mixed micelle formulation.

28. The method of Claim 27, wherein said formulation comprises: akali metal C_8-C_{22} alkyl sulfate, a pharmaceutically acceptable edetate, at least one alkali metal salicylate, and at least one micelle forming compound selected from the group consisting of lecithin, hyaluronic acid, pharmaceutically acceptable salts of hyaluronic acid, octylphenoxypolyethoxyethanol, glycolic acid, lactic acid, chamomile extract, cucumber extract, oleic acid, linolenic acid, borage oil, evening of primrose oil, menthol, trihydroxy oxo cholanylglycine and pharmaceutically acceptable salts thereof, glycerine, polyglycerin, lysine, polylysine, polidocanol alkyl ethers and analogues thereof, triolein and mixtures thereof; wherein each of said sulfate, edetate and salicylate is present in a concentration of from 1 to 10 wt./wt.% of the total formulation, and wherein each micelle forming compound is present in a concentration of from 1 to 10 wt./wt.% of the total formulation, and the total concentration of sulfate, edetate, salicylate, and micelle forming compounds is less than 50 wt./wt.% of the formulation

29. The method of Claim 27, wherein said micelles are 1 to 10 nm in size.

30. The method of Claim 28, wherein said alkali metal C_8-C_{22} sulfate is sodium lauryl sulfate.

31. The method of Claim 28, wherein said edetate is an alkali metal edetate.

32. The method of Claim 28, wherein said alkali metal salicylate is sodium salicylate.

33. The method of Claim 28, wherein said micelle forming compound is lecithin, lecithin in combination with hyaluronic acid, evening of

primrose oil or borage oil.

34. The method of Claim 28, wherein said formulation comprises a combination selected from the group consisting of: i) sodium lauryl sulphate, sodium salicylate, disodium edetate, saturated phospholipid and sodium hyaluronate; ii) sodium lauryl sulphate, sodium salicylate, disodium edetate, lecithin and sodium hyaluronate; iii) sodium lauryl sulphate, sodium salicylate, disodium edetate, sodium hyaluronate and evening of primrose oil; iv) sodium lauryl sulphate, sodium salicylate, disodium edetate, saturated phospholipid and bacitracin; v) sodium lauryl sulphate, sodium salicylate, disodium edetate, saturated phospholipid, sodium hyaluronate and bacitracin; and vi) sodium lauryl sulfate, sodium salicylate, disodium edetate, sodium hyaluronate, oleic acid and gamma linoleic acid.

36. The method of Claim 28, wherein said mixed micelle formulation further comprises water.

37. The method of Claim 26, wherein said insulin is administered in solution.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application Of	: Group Art Unit: 1615
PANKAJ MODI	: Examiner: T. Ware
Serial No. 09/538,829	: Attorney Docket No. 358594-00010-2
Filed: March 30, 2000	: Entitled:
	: METHOD FOR ADMINISTERING INSULIN TO THE BUCCAL REGION

DECLARATION OF PANKAJ MODI

I, Pankaj Modi, being duly sworn hereby declare as follows:

1. I have a Master of Science degree in Chemical Engineering (Brooklyn Polytechnic University, U.S.A., 1976); a Master of Science degree in Polymeric Materials / Biomedical Sciences (Brooklyn Polytechnic University, U.S.A., 1976); a Master of Business Administration degree (University of Dallas, U.S.A., 1978); and a Doctorate (Ph.D.) in Biomedical Sciences / Biopolymeric Materials (University of Toronto, 1992). I did additional Post-Doctorate training at McMaster University in the Department of Neuroscience / Psychiatry.

2. Since October of 1996 to the present I have been employed at Generex Pharmaceuticals, Inc., 22 Harbour Square, Suite 202, Toronto, Ontario, Canada M5J 2G2 where I am Vice President of Research and Development. In my position as Vice President of Research and Development, I am responsible for, among other things, new drug development, including all testing (including oversight of clinical trials) associated with new drug development.

3. From 1994 (prior to the time I joined Generex Pharmaceuticals, Inc.) to the present, I have been involved in the research and development of novel drug delivery systems. I have developed various delivery systems for oral and/or nasal delivery of drugs including non-steroidal anti-inflammatories, vaccines, interferons and hormones and other pharmaceutical agents to be used in the treatment of a variety of diseases. A primary focus of my research while at Generex has been

the development of an oral delivery system for insulin and other large molecule drugs.

4. I am a member of the following professional societies: American Diabetes Association; Canadian Diabetes Association; Society of Endocrinology; American Association of Pharmaceutical Scientists; Indian Association of Pharmaceutical Scientists; and the Professional Chemical Engineers Society.

5. I have been a named inventor on 19 U.S. patents/patent applications.

6. I am the named inventor of the invention set forth in the claims of the above-captioned application

7. I participated in the preparation of the above-captioned application and claims, read the same thoroughly before the case was filed, and I have recently re-read and reviewed the application and claims of the case.

8. I have carefully read the Office Action dated July 12, 2001, which included rejection of the claims under 35 U.S.C. § 102(e) as anticipated by Manning et al. (5,770,559), and the rejection of the claims under 35 U.S.C. § 103(a) as obvious in view of the Manning and Radhakrishnan (5,049,389) references.

9. The present invention is directed to a method for delivering insulin compositions to the buccal region of the oral cavity. According to the methods of the present invention, a patient self-administering the insulin composition will resist inhalation of the spray, to ensure delivery of the drug to the buccal region. When inhalation is resisted, over 80 percent of the aerosol is delivered to the oral cavity; less than 10% is delivered to the gastrointestinal tract or the lungs (some of the formulation remains in the device).

10. As is known to anyone developing new modes of insulin delivery for diabetics, delivery of insulin requires very precise dosage. Delivery of too much insulin can result in hyperglycemic shock; delivery of too little insulin results in the opposite, hypoglycemic shock. Either situation can be life-threatening. Thus, it is essential that any mode deliver a predictable and known amount of the drug. A method in which the residual dose from a completely different method of administration (to the lungs) may or may not be delivered to the buccal cavity, where it may or may not be absorbed, is not a method which can reliably deliver an effective

amount of insulin. Therefore, the method of the '559 patent cannot be said to teach delivery, either explicitly or inherently, of an effective amount of insulin to the buccal cavity.

11. The '559 patent discloses at column 15, lines 15-20, significant lung absorption, that is, greater than 80% of the formulation is utilized in the lungs. Therefore, the less than 20% remaining, a portion of which may still reside in the device itself, cannot be considered an effective amount of the drug, for purposes of the present invention. As noted above, delivery of an effective amount of insulin requires a precise and known amount of the drug.

12. The '559 patent discloses delivery of the formulation described therein to the lungs. With this mode of delivery, patients do not resist inhalation; on the contrary, they inhale as deeply as possible to draw the drug into the lungs. Patients receiving the drugs described in the '559 patent could not resist inhalation of the drug and receive an effective dose according to the methods of that invention.

13. In view of the fact that the method of administration described in the '559 patent requires inhalation of the composition, the '559 patent cannot be said to teach or suggest resisting inhalation, as recited in the claims of the present invention; in fact, it teaches the opposite. Similarly, the method of the '559 patent cannot result, either explicitly or inherently, in an effective amount of the drug being delivered to the buccal region of the oral cavity of a patient. It is my well considered opinion, therefore, that the '559 patent does not anticipate the claims of the present invention; it does not teach or suggest delivery of an effective amount of the drug to the buccal region of the oral cavity, while resisting inhalation.

14. The claims of the present invention were also rejected as obvious in view of the '559 patent. However, as described above, the '559 patent does not teach or suggest, either explicitly or inherently, that an effective amount of insulin can be delivered to the buccal region, while resisting inhalation. The '559 patent teaches lung delivery of the compositions therein; such delivery would require inhalation of the formulation and could not be administered to someone who was resisting inhalation.

15. The claims of the present invention were also rejected as obvious in view of the '389 patent. It is my well considered opinion, that this patent does not render obvious, the claims of the present invention.

16. As in the '559 patent, the '389 patent discloses delivery of a formulation to the lungs. Patients receiving the formulation described therein would not resist inhalation; they would inhale as deeply as possible to draw the drug into their lungs. Patients receiving the drugs described in the '389 patent could not resist inhalation of the drugs and receive an effective dose.

17. The examples of the '389 patent show that the majority of the drug is successfully administered to the lung, including the deep lung region. Table 9 of the '389 patent indicates that less than 20% of the formulation remains in the joint, throat or collar of the device, areas which *may* correspond to the oral cavity of a person, or alternatively, to residual amounts left in a device used by a patient. Therefore, the small amount remaining in the device cannot be considered an effective amount of the drug for purposes of the present invention.

18. In view of the above, the '389 patent does not teach or suggest spraying a composition while resisting inhalation, nor does it teach or suggest, explicitly or inherently, delivery of an effective amount of insulin to the buccal region. Therefore, it is my well considered opinion that the '389 patent does not render obvious the claims of the present invention.

19. Based on all of the above, it is my well considered opinion that the claims of the present invention are patentable over the '559 and '389 patents.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated: Nov. 12, 2001 Pankaj Modi

Pankaj Modi

JAMESBURY CORP., Appellant v. LITTON INDUSTRIAL PRODUCTS, INC., Appellee

No. 84-1079

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

756 F.2d 1556; 1985 U.S. App. LEXIS 14740; 225 U.S.P.Q. (BNA) 253

March 12, 1985

PRIOR HISTORY:{**1}

Appealed from: U.S. District Court for the District of Connecticut.

COUNSEL: Robert C. Miller, Oblon, Fisher, Spivak, McClelland and Maier, P.C., of Arlington, Virginia, argued for Appellant. With him on the brief was Arthur I. Neustadt.

Donald R. Dunner, Finnigan, Henderson, Farabow, Garrett and Dunner, of Washington, District of Columbia, argued for Appellee.

Allen M. Sokal, Finnigan, Henderson, Farabow, Garrett and Dunner, of Washington, District of Columbia, of Counsel.

Spencer T. Smith, of Hartford, Connecticut, on the brief for Appellee.

JUDGES: Nies, Newman and Bissell, Circuit Judges.

OPINIONBY:NIES

OPINION:{*1557} NIES, Circuit Judge.

Jamesbury Corp., the plaintiff below, charged Litton Industrial Products with infringing claims 7 and 8 of its U.S. Patent No. **2,945,666**to Freeman entitled "Ball Valve." n1 Following a seven day jury trial, the jury returned a verdict for Litton, concluding, in answer to an interrogatory, that the asserted claims did not differ in any "significant particulars" fromthe prior art. n2 Under the court's instructions, this finding meant that the claims were invalid under **35 U.S.C. §102**(a) n3 for lack of novelty. Jamesbury had timely {**2} objected to the jury charge on the issue of novelty and tothe wording of the particular interrogatory under review,as well as to other instructions. No instructions were given with respect to obviousness of the claimed inventions,Litton having agreed that obviousness was not asserted asa ground for holding the claims invalid. Following entry of judgment, Jamesbury filed a motion under Fed. R. Civ. P. 50(b) for judgment notwithstanding the verdict, which was denied by the district court. In ruling on the motion, the district court stated:

> {*1558} The jury returned a verdict for the defendant in this patent infringement suit. The plaintiff has movedfor judgment notwithstanding the verdict. The plaintiff is seeking judgment on all disputed issues: the validity ofthe patent, infringement of the patent, the amount of damages, and the defenses of laches and estoppel. In its response to a special interrogatory, the jury made explicit its finding that the patent was invalid because of lack of novelty over the prior art. Thus the crucial issue to be resolved is whether the jury's finding of invalidity shouldbe set aside. Judgment n.o.v. should only be granted when: {**3}
>
> > (1) there is such a complete absence of evidence supporting the verdict that the jury's findings could only have been the result of sheer surmise and conjecture, or (2) there is such an overwhelming amount of evidence in favor of the movant that reasonable and fair minded men could not arrive at a verdict against him.

***Mattivi v. South African Marine Corp.*, 618 F.2d 163, 168 (2d Cir. 1980).**Neither of the tests for judgment n.o.v. is satisfied by the plaintiff's motion. The plaintiff alleges that the defendant has produced no evidence regarding the level of ordinary skill in the ball valve art. Although such proof is essential to support a finding of invalidity because of obviousness, ***see Environmental Designs v. Union Oil Co.*, 713 F.2d 693, 695, 218 U.S.P.Q. (BNA) 865 (Fed. Cir. 1983),**the plaintiff has cited no authority requiring such proofto support a finding of invalidity because of lack of novelty over the prior art. On the issue of novelty, there was ample evidence to support the jury's verdict; there wascertainly not an overwhelming amount of evidence in the plaintiff's favor that reasonable and

fair minded men couldnot arrive at a verdict {**4} against it. For the foregoing reasons, the motion for judgment n.o.v. is denied.

- - -Footnotes- - -

n1 This case has been twice before the United States District Court for the District of Connecticut, and once beforethe United States Court of Appeals for the Second Circuit. ***Jamesbury Corp. v. Litton Industrial Products, Inc.*, 442 F. Supp. 266, 196 U.S.P.Q. (BNA) 544 (D. Conn. 1977),*rev'd*, 586 F.2d 917, 199 U.S.P.Q. (BNA) 641 (2d Cir. 1978),*cert. denied*, 440 U.S. 961, 59 L. Ed. 2d 774, 99 S. Ct. 1503, 201 U.S.P.Q. (BNA) 960 (1979).**In the first district court decision on Litton's motion for summary judgment, claims 7 and 8 were held invalid for "overclaiming", that is, for claiming an entire ball valverather than simply an improved sealing ring in the valve.On appeal to the Second Circuit, the "overclaiming" defense was rejected and the case remanded for trial. The technical subject matter of the claims on appeal has been adequately described in these opinions, and familiarity with the discussion contained therein will be presumed. This opinion contains only such background as is necessary for anunderstanding of the position of the parties on appeal.

{**5}

n2 Jury interrogatory No. 1 reads as follows:

> 1. Does the ball valve construction shown and described in the Saunders British patent or any other prior art differ in any significant particulars from the ball valve defined by the express language of claims 7 and 8 of the Freeman patent? As to claim 7 Yes No XAs to claim 8 Yes No XIf you answer "No" as to both claim 7 and claim 8, do notanswer any further questions.

The remaining questions were directed to infringement, laches, estoppel and damages. In accordance with the above direction, the jury answered only interrogatory No. 1.

n3 **35 U.S.C. §102**(a) reads:

> A person shall be entitled to a patent unless -- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patents. . . .

- - -End Footnotes- - -

In this appeal, Jamesbury argues that because of erroneousand prejudicial error in the instructions to the jury, itis entitled at least to a new trial. Jamesbury {**6} further asserts that because lack of novelty was not established and other grounds asserted for holding the claims invalid, namely, obviousness and inequitable conduct, were withdrawn or waived, the court erred in its ruling on Jamesbury's motion JNOV. We agree and, therefore, reverse theholding of invalidity of claims 7 and 8. The case is remanded for resolution of other issues.

II.

The standard of review of instructions is prejudicial legal error. ***Railroad Dynamics, Inc. v. A. Stucki Co.*, 727 F.2d 1506, 1512, 220 U.S.P.Q. (BNA) 929, 939 (Fed. Cir. 1984).**

A.

Jamesbury first attacks the following instruction which laid the foundation for the jury's deliberations:

> The public is a silent but nevertheless an important, an interested party in all patent litigation and it is entitled to protection against the monopolization of what is not lawfully patentable. In other words, it's not simply between Jamesbury and Litton. Other people are affected by it. So I charge you that it is your duty to *subject the invention*defined in claims seven and eight of the Freeman patent *to careful scrutiny before endorsing Jamesbury's right to the patent monopoly*defined {**7} by such claims. [Emphasis added.]

Jamesbury argues that the effect of this instruction was to create a presumption of invalidity requiring Jamesbury to prove, beyond careful scrutiny, that it was en-

titled to maintain a monopoly, which, impliedly, was against the public interest. We agree that this instruction is legally erroneous and prejudicial.

The language that the jury must give "careful scrutiny" before "endorsing" the "patent monopoly" cannot be approved.{*1559} While the language does not rise to the levelof a presumption of invalidity, it does incorrectly suggest that the jury must affirmatively find the patent valid,which is never appropriate. ***See Envirotech Corp. v. Al George, Inc.*, 730 F.2d 753, 762, 221 U.S.P.Q. (BNA) 473, 480 (Fed. Cir. 1984)**("court never 'declares' a patent valid").

Further, this court has disapproved of a challenger's characterization of a patentee by the term "monopolist", whichis commonly regarded as pejorative. ***Union Carbide Corp. v. American Can Co.*, 724 F.2d 1567, 1574, 220 U.S.P.Q. 584, 590 n. 4 (Fed. Cir. 1984);*Carl Schenck A.G. v. Norton Corp.*, 713 F.2d 782, 784, 218 U.S.P.Q. 698, 699 (Fed. Cir. 1983).**{**8} In both of the cited cases, a bench trial was involved. Here, not only was Litton's counsel not admonished for so characterizing Jamesbury before the jury, a more serious impropriety than in a bench trial, but also the characterization found its way into the instructions. As stated in ***Connell v. Sears, Roebuck &Co.*, 722 F.2d 1542, 1548, 220 U.S.P.Q. (BNA) 193, 198 (Fed. Cir. 1983),**the characterization of a patent as a "monopoly" is misdirected:

> The phrase "patent monopoly" appears at various points. Under the statute, **35 U.S.C. §261,**a patent is a form of property right, and the right to exclude recognized in a patent is but the essence of the concept of property. ***Schenck v. Nortron Corp.*, 713 F.2d 782, 218 U.S.P.Q. (BNA) 698 (Fed. Cir. 1983).**

Instructions which supplement the statutory body of law governing patent validity by interjecting language to the effect that the public must be "protected" against a "monopoly," a term found nowhere in the statute, are likely to beprejudicial and should be avoided.

B.

This court has repeatedly held that the facts leading to aconclusion of invalidity must be established by clear andconvincing evidence. {**9} ***See, e.g., American Hoist &Derrick Co. v. Sowa &Sons, Inc.*, 725 F.2d 1350, 1360, 220 U.S.P.Q. (BNA) 763, 771 (Fed. Cir. 1984)**and its progeny. This standard is unvarying. Therefore,Jamesbury correctly asserts that error was committed by the district court in giving the following instruction to the jury:

> If you find that to be so *by a preponderance of the evidence*, that the Saunders British patent or other prior art disclosed substantially the same things as set forth in Freeman's claims 7 and 8 and in the same scope as here asserted for infringement purposes, then such claims 7 and 8 are void for lack of novelty. [Emphasis added.]

Litton responds that elsewhere in the instructions, the jury was instructed on the "clear and convincing" standard of proof.

The record shows that the jury was charged at the close ofone day's proceedings. Prior to beginning its deliberations the next day, after discussions with counsel, the court reinstructed the jury that the defendant had the burden of proving by clear and convincing evidence that the Patent and Trademark Office (PTO) was wrong in issuing the patent. The court then went on to instruct that where {**10}certain prior art was not considered by the PTO, or if the PTO was misled with respect to what a reference meant, then the burden was merely a preponderance of the evidence. Further, the court advised that, if the patentee were guilty of fraud (despite the absence of a fraud defense in this case), the plaintiff would have to prove that its patent was valid. n4 Finally, the court summed up as follows:

> There's a presumption it [patent] was valid. Can be overcome by clear and convincing proof if certain prior art was not considered. It can be overcome merely by a preponderance of the evidence {*1560} if the patent examiner was misled as to the meaning of that prior art.

- - -Footnotes- - -

n4 In connection with the inequitable conduct defense, we observe that even though expressly withdrawn, the operation of that defense was described to the jury. Under these circumstances, reference in the instructions to a patent owner misleading the examiner was prejudicial. Further, expanding the jury's general knowledge of legal matters not material to the trial does nothing to enhance the jury's comprehension or the proper administration of justice.

- - -End Footnotes- - -

{**11}

If we assume the transcription is correct, this additionalinstruction is at best confusing and continues to erroneously vary the quantum of proof depending on the circumstances in contravention of the precedent of this court. Contrary to Litton's argument, an instruction that is defective because of a misstatement of law is not cured simply by a correct statement appearing elsewhere. More is requiredof jury instructions than to state the law correctly somewhere in the instructions. The question, once a misstatement has been made, is whether the error was so egregious, considering the instructions as a whole, as to require theverdict to be set aside. In this case we hold that it was.

C.

Jamesbury's objections (also made to the district court) that the instructions and interrogatory No. 1, reproduced at note 2, *supra*, misstate the law respecting novelty were legitimate. The instruction (quoted in B above) to the effect that the claims are invalid if the prior art Saunders patent discloses "substantially the same things" as claims 7 and 8, and Interrogatory No. 1 which speaks of the claims not differing in "significant particulars", are not legally correct.

The error {**12} in this interpretation of the statutory requirement of novelty is the same as that which was addressed in ***Connell*, 722 F.2d at 1548, 220 U.S.P.Q. at 198:**

> The opinion says anticipation may be shown by less than "complete anticipation" if one of ordinary skill may in reliance on the prior art "complete the work required for theinvention", and that "it is sufficient for an anticipation 'if the general aspects are the same and the differencesin minor matters is only such as would suggest itself to one of ordinary skill in the art.'" Those statements relate to obviousness, not anticipation. Anticipation requires the presence in a single prior art disclosure of all elements of a claimed invention arranged as in the claim. ***Soundscriber Corp. v. U.S.*, 175 Ct. Cl. 644, 360 F.2d 954, 960, 148 U.S.P.Q. (BNA) 298, 301, 149 U.S.P.Q. (BNA) 640 (1966).**A prior art disclosure that "almost" meets that standard may render the claim invalid under §103; it does not "anticipate."

Here, as well, anticipation is not shown by a prior art disclosure which is only "substantially the same" as the claimed invention.

Litton argues that elsewhere the district court amplified its {**13} interpretation by speaking of the prior art disclosing the claimed invention "in complete terms." However, that additional paragraph of instructions also speaksof "*substantially*the same subject matter . . . *in complete terms, thus enabling*a man skilled in the art to understand and practice the invention." We see no correction of the legal standard in the above statement.

III.

Because of the above legal errors, the verdict of invalidity for lack of novelty (i.e., anticipation) cannot stand.Jamesbury would be entitled to a new trial as a result of those legal errors; Jamesbury moved, however, for judgment NOV. We will, accordingly, turn to the question of whether Jamesbury was entitled to judgment NOV considering theevidence under the proper legal standard of **35 U.S.C. §102.**As stated in ***Connell*, 722 F.2d at 1546, 220 U.S.P.Q. at 197:**

> The court must inquire, under the proper legal standard of patentability, whether the evidence and inferencesreasonably drawn therefrom, when viewed in the light most-favorable to the non-moving party and without weighing credibility, is or is not substantial. [Citation omitted.]

Accordingly, we must determine {**14} whether there exists evidence of record upon which a jury might properly have returned a verdict in Litton's favor when the correct legal standard is applied. If there is not, Jamesbury was entitled to have the question removed from the jury and decided as a matter of law. 9 Wright {*1561} &Miller, *Federal Practice &Procedure: Civil*§2524 (1972). The standard of review by a court of appeals is the same. The question of whether the evidence is sufficient to create an issue of fact for the jury is itselfa question of law, which we will now decide. *Id.*

The precise question here is whether reasonable persons could conclude that Litton proved by clear and convincing evidence that each and every limitation of claim 7 and 8 is disclosed by Saunders.

The claims in suit are the following:

> 7. A ball valve comprising: a casing adapted to be connected to a pipe line and having a valve chamber and inlet and outlet openings; a ball mounted in said chamber and having a port; and a sealing ring mounted in said chamber around one of said openings, *said ring having a lip projecting inward toward the axis of the ring and engaging the ball, said lip being free to bend*{**15} *in the axial direction of the*

> *ring and increasing in thickness outward in the radial direction of the ring*, and said ball being rotatable between an open position in which said port is in register with the opening surrounded by said ring and a closed position. [Emphasis added.] 8. A ball valve as described in claim 7, said lip having side faces disposed one toward the ball and one away from the ball, and said faces diverging from each other substantially uniformly outward in the radial direction of the ring.

Litton does not dispute that the claim language "a lip . .. engaging the ball" means, in light of the specification, that the lip is "pushing against the ball." In the wordsof the Second Circuit in the previous appeal of this case:

> The seal, which is given a more technical description in claims 7 and 8, has a lip which remains in constant contact with the ball, which may flex to permit rotation and reduce wear, but which is so constructed and placed that it remains tight against the surface of the ball at all times.

199 U.S.P.Q. at 643.

Freeman accomplishes this constant tight contact by a lip on the seal or ring which interferes with {**16} the placement of the ball. The lip protrudes into the area wherethe ball will be placed and is, thus, deflected after theball is assembled into the valve. Thus: (SEE FIG. 5 AND 6IN ORIGINAL)

Because of this constant pressure, the Freeman valve is described as providing a particularly good seal when regulating a low pressure stream.

Nothing in Saunders discloses the lip in one position before assembly with the ball and in a deflected position after the ball is in position. Specifically, Saunders teaches"a narrow flange-like portion to the back of which the fluid pressure has access so pressing this portion against the plug [ball]" and that the ring (but not specifically {*1562} the lip or flange) is "in engagement with the spherical plug [ball] surface."

The disclosed structure in Saunders is different from thatin Jamesbury. As shown in the patent and as more clearlyrepresented by Litton, Saunders shows:

[SEE ILLUSTRATION IN ORIGINAL]

The Saunders specification further states, "It will be observed that the fluid pressure [from left to right] will act mainly on the inner flange-like portion of the ring [14]which is relatively flexible and will {**17} thereforebe pressed *by the fluid pressure*into good contact with the valve plug [1]." (Emphasis added.) Saunders speaks of improving the seal as the pressureincreases.

Nevertheless, relying on the testimony of its expert witness, Professor Youngdahl, Litton maintains that Saunders meets the claim limitation as interpreted to mean constant contact of the lip in a sealing engagement with the ball. His testimony is as follows:

> If that ball were removed, if a Saunders type seal were put in the position so that the, it engaged the body and then the end cap were bolted up, the Saunders lip would bend away from the end cap increasing the gap that's there and move toward where the ball would be. Of course, when you put the ball in and bolt it up with the ball, you're going to push that lip back. But bending it forward means that it springs that way. Then when you put the ball in and bend it back you have a preloading of the lip and the ball (indicating).

Dr. Youngdahl also testified that he made a model which disclosed this phenomena. Jamesbury's witness disputed the accuracy of the model as a representation of Saunders.

Jamesbury's witnesses testified {**18} that the disclosure of Saunders shows no preload or interference between the Saunders flange or lip and the ball, the lip merely touching the ball; that the seal or joint occurs below the lip in the main body of the ring; that under pressure the lip pushes the ball to make a better seal in the main body (compression seating area); and that the lip only sealinglyengages the ball when under pressure.

Saunders was considered by the PTO during examination and by the U.S. Court of Claims in an infringement suit on thesame claims 7 and 8 against the government. ***Jamesbury Corp. v. United States*, 207 Ct. Cl. 516, 518 F.2d 1384, 187 U.S.P.Q. (BNA) 720 (1975).**Litton, through its Contromatics division, was one of thegovernment's suppliers of the infringing valve. n5 Both the PTO and the Court of Claims concluded that claims 7 and8 were patentable over the Saunders reference. The Courtof Claims held, specifically, that Freeman claims 7 and 8were neither anticipated by nor obvious from Saunders. This decision was based on a finding that:

> The term "engaging the ball" recited in claims 7 and 8 means that the lip contacts

the ball with sufficient force to {*1563} provide {**19} a fluid tight seal. . . . The Saunders flange or lip only sealingly engages the ball 1 on the upstream side when the fluid pressure forces the lip against the ball and never sealingly engages the ball on the downstream side because there is no fluid pressure there to force the lip against the ball. The Saunders sealing ring provides a compression type of seal whichdepends upon the ball pressing into the material of the ring. * * * The seal of Saunders depends primarily on the contact between the ball and the body of the sealing ring, and the flange or lip sealingly contacts the ball on the upstream side when the fluid pressure increases.

207 Ct. Cl. 516, 551-52.

- - -Footnotes- - -

n5 This suit concerns non-government sales.

- - -End Footnotes- - -

Dr. Youngdahl's explanation for the allowance of those claims was, "I don't believe that anyone ever explained the action of the Saunders seat to them and that they understood that there was a preload." Further, Litton asserts that Jamesbury misrepresented to the PTO that a patentable difference {**20} existed between Freeman and Saunders in "that the upstream sealing ring of Saunders' ball valve would leak, whereas the upstream Jamesbury sealing ring wouldnot leak." The Youngdahl model assertedly showed that there was no leak.

The issue, of course, is not whether Saunders' valve leaksor does not leak, but whether Saunders discloses a lip which sealingly engages the ball, i.e., whether the Saunderslip functions as the claim limitation requires and whether reasonable persons would find the evidence clear and convincing that it does meet the claim. ***SSIH Equipment S.A. v. U.S. International Trade Commission*, 718 F.2d 365, 383, 218 U.S.P.Q. (BNA) 678, 693 (Fed. Cir. 1983)**(Nies, J., additional views).

Litton argues that the testimony of its expert, Dr. Youngdahl, which was not before the PTO or the Court of Claims, to the effect that this limitation is found in Saunders issubstantial evidence of anticipation. Jamesbury argues that the record as a whole including the unchallenged testimony discrediting Dr. Youngdahl's model of Saunders resultsin no evidence on which a reasonable jury could find anticipation, particularly in view of the consideration of theCourt of Claims {**21} and the PTO of the same art. While the decisions of the examiner and the Court of Claimsare, of course, not binding in this litigation, we conclude that Dr. Youngdahl's testimony with respect to Saundersis not of such character, when viewed with the reference itself and the contrary testimony of the Jamesbury witnesses, as to overcome clearly and convincingly the presumption of validity, **35 U.S.C. §282.**Nor does it persuade us that deference is not due the full and careful analysis by the Court of Claims and its determination that the *lip*in Saunders does not sealingly engage the ball at all times. The meticulous opinion of then Commissioner Lane n6 indicates full comprehension of how the valves work. Thus,Dr. Youngdahl's testimony is not substantial evidence, inview of the record as a whole, to support a determinationof invalidity for lack of novelty.

- - -Footnotes- - -

n6 The Court of Claims adopted the opinion of then Commissioner Donald E. Lane (reported at **153 U.S.P.Q. (BNA) 672 (1967)),**who was later (1969-1979) a judge on the U.S. Court of Customs and Patent Appeals, one of our predecessor courts.

- - -End Footnotes- - -

{**22}

Since a reference which does not satisfy one limitation ofa claim does not anticipate, we need not address in detail the arguments of Jamesbury concerning other missing elements in Saunders. We observe, however, that at least one additional limitation of claim 7 is not disclosed therein.

In particular, claim 7 requires that the lip be "increasing in thickness outward in the radial direction of the ring. " Referring to Figures 5 and 6 of the **'666**patent, reproduced *supra*, the specification defines "lip" as follows:

> The part of the ring [25] which first engages the ball [27] is a free standing interior lip 25c having a rounded inner surface 25d, and an oblique surface 25e. Leading to the lip is an oblique surface {*1564} 25f on which the ball will eventually be seated when the lip is deflected sufficiently under load.

Thus, when read in light of the specification, the claimedlimitation that the lip increase in thickness outward reads

upon the embodiment illustrated in Figures 5 and 6. When this definition of "lip" is compared to the Saunders device, the claim limitation is simply not met. Instead of "increasing in thickness outward" as required {**23} inthe claim, the properly defined lip portion in Saunders does not change in thickness along its radial axis. It is unimportant that Litton has found a way to redefine "lip" in terms which encompass the Saunders device, since we arecompelled to seek such guidance from the specification, and not from the accused infringer.

With respect to claim 8, Litton's witness acknowledged that the geometry of the two lips, which is what the claim specifies, is different.

With respect to other validity issues, Litton specificallywithdrew its request for an instruction on obviousness ofthe claims. The following colloquy occurred during the district court's review of Litton's requested instructions:

> The Court: I think Youngdahl, Professor Youngdahl said this isn't any different than Saunders. He didn't sayit's something that's obvious and *so I don't know that any obviousness ever came into play in this case*. You're nodding your head. MR. SMITH [for Litton]: *No, it didn't*. The Court: Mr. Smith, so -- MR. SMITH: *I agree*. The Court: If you agree then I guess I won't have any difficulty with -- 35 is out, for one reason, and then 35 through 37, they all deal {**24} with obviousness. [Emphasis added.]

In this appeal, Litton did not assert that, if the judgment were to be overturned, Litton was entitled to retry obviousness. Under the circumstances, the issues of obviousness of claims 7 and 8 have been waived.

In view of the absence of sufficient evidence to support aholding of invalidity on the ground of anticipation, and the withdrawal of alternative attacks on the patent, we conclude that the district court erred in failing to grant Jamesbury's motion for JNOV with respect to validity of claims 7 and 8. Accordingly, the court's ruling on the motion must be reversed.

IV.

Because the issues of infringement, laches and estoppel were not resolved at the conclusion of the trial, the case must be remanded for their disposition. The decision of this court in *Envirotech Corp.*provides guidance on proper instructions if the issue of infringement is again tried to a jury. As stated therein:

> In general, a finding of infringement depends on whether the accused device falls within the scope of the asserted claims as properly interpreted. ***Kalman v. Kimberly-Clark Corp.*, 713 F.2d 760, 770, 218 U.S.P.Q. (BNA) 781, 788 (Fed. {**25} Cir. 1983).**The patented invention as indicated by the language of the claims must first be defined (a question of law), and then the trier must judge whether the claims cover the accused device (a question of fact). ***See Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1569, 219 U.S.P.Q. (BNA) 1137, 1140 (Fed.Cir. 1983);*SSIH Equipment S.A. v. USITC*, 718 F.2d 365, 375, 218 U.S.P.Q. (BNA) 678, 688 (Fed. Cir. 1983).**The patent owner must show by a preponderance of the evidence that the accused [device] has infringed his patent. ***Hughes Aircraft v. United States*, 717 F.2d 1351, 1361, 219 U.S.P.Q. (BNA) 473, 480 (Fed. Cir. 1983);*SSIH, supra*;**Chisum, *Patents*, 18.06[1] (1983).

730 F.2d at 758, 221 U.S.P.Q. at 477.

Further, the instructions should be tailored to the dispute in this case. As stated in ***Structural Rubber Products Co. v. Park Rubber Co.*, 749 F.2d 707, 723, 223 U.S.P.Q. (BNA) 1264, 1276 (Fed. Cir. 1984):**

> We join other courts that have held that the duty of a trial court in any jury trial is to give instructions which are meaningful, not in terms of some abstract {*1565} case, but which can be understood and given effect {**26}by the jury once it resolves the issues of fact which are in dispute. ***See, e.g., Choy v. Bouchelle*, 436 F.2d 319 (3rd Cir. 1970);*Marshall v. Isthmian Lines, Inc.*, 334 F.2d 131, 138 n. 15 (5th Cir. 1964).**

Thus, the court should instruct the jury on what the claimmeans in light of this decision and instruct what elements of the claim are disputed to be found in the Litton valves literally or under the doctrine of equivalents.

Conclusion

For the foregoing reasons, the judgment is *reversed*and the case is *remanded*for disposition of all remaining issues other than the validity of claims 7 and 8 of Freeman Patent No. **2,945,666.**

REVERSED AND REMANDED

IN RE ALBERT M.A. RIJCKAERT and JOANNES A.E. VAN DER KOP

93-1206

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

9 F.3d 1531; 1993 U.S. App. LEXIS 30162; 28 U.S.P.Q.2D (BNA) 1955

November 23, 1993, Decided

PRIOR HISTORY:{**1} Appealed from: U.S. Patents and Trademark Office Board of Patent Appeals and Interferences

DISPOSITION:REVERSED

COUNSEL: Edward W. Goodman, North American Philips Corporation, ofTarrytown, New York, argued for appellant. With him on the brief was Algy Tamoshunas.

Lee E. Barrett, Associate Solicitor, Office of the Solicitor, of Arlington, Virginia, argued for appellee. With him on the brief was Fred E. McKelvey, Solicitor.

JUDGES: Before MAYER and LOURIE, Circuit Judges, and LAY, * Senior Circuit Judge.

> * Honorable Donald P. Lay, Senior Circuit Judge, United States Court of Appeals for the Eighth Circuit, sitting by designation.

OPINIONBY:LOURIE

OPINION:

{*1531} LOURIE, Circuit Judge.

Albert Rijckaert and Joannes van der Kop ("Rijckaert") appeal from the decision of the United States Patent and Trademark Office (PTO), Board of Patent Appeals and Interferences affirming the final rejection of claims 5-12, all of the pending claims in patent application serial no. 07/345,396, as being unpatentable under **35 U.S.C. §103**(1988). Because the references relied upon to reject {*1532} the claims do not provide the basis for a prima faciedetermination that the claimed invention would have been obvious, {**2} we reverse.

BACKGROUND

The patent application at issue relates to an apparatus for recording and reproducing an electric signal on a magnetic record carrier. Independent claim 11 is drawn to a recording apparatus and it specifies a relationship between time expansion or compression and three variables a, n, and M. Claim 11 reads, in pertinent part:

> 11. An apparatus for recording an electric signal on a magnetic record carrier in tracks which are inclined relative to the longitudinal direction of said record carrier, comprising: . . . . . [a] time-base correctioncircuit providing a time expansion or time compression ofthe signal blocks by a factor of a*n/(180*(M+1)), where ais the wrapping angle of the record carrier around the head drum and differs from 180 degrees, n is the number of head pairs, and M is the number of times within a specific time interval that a head pair which comes in contact withthe record carrier during said time interval does not record a signal on the record carrier, said time interval being defined by those instants at which two consecutive track pairs are recorded by one or two head pairs.

Independent claim 12 is drawn to an apparatus {**3} forreproducing a recorded signal and it recites the reciprocal relationship between time compression or expansion and the three variables a, n, and M. Dependent claims 5-10 further limit claims 11 or 12.

The Board upheld the final rejection of claims 5 and 7-12 under **35 U.S.C. §103**as being unpatentable over U.S. Patent **4,757,392**to Awamoto in view of Driessen et al., An Experimental Digital Video Recording System,CE-32 I.E.E.E. Transactions on Consumer Electronics 3, Aug. 1986, at 362-70. The Board also upheld the final rejection of claim 6 as being unpatentable over Awamoto and Driessen in view of U.S. Patent **4,542,417**to Ohta.

DISCUSSION

We review de novothe Board's ultimate determination of obviousness. **In re De Blauwe, 736 F.2d 699, 703, 222 USPQ 191, 195 (Fed. Cir. 1984).**Underlying factual inquiries, such as the scope and content of the prior art, differences between the prior art andthe claimed invention, and level of ordinary skill in theart are reviewed for clear error. See **In re Caveney, 761 F.2d 671, 674, 226 USPQ 1, 3 (Fed. Cir. 1985).**{**4}

In rejecting claims under **35 U.S.C. §103,**the examiner

bears the initial burden of presenting a prima faciecase of obviousness. **In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992).**Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant. Id."A prima faciecase of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art." **In re Bell, 991 F.2d 781, 782, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993)**(quoting **In re Rinehart, 531 F.2d 1048, 1051, 189 USPQ 143, 147 (CCPA 1976)).**If the examiner fails to establish a prima faciecase, the rejection is improper and will be overturned. **In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988).**

All of the claims except claim 6 stand rejected under **35 U.S.C. §103**as being obvious {**5} over Awamoto in view of Driessen. n1 Awamoto, the primary reference, discloses a signal processing circuit for a video recording and reproducing apparatus. Awamoto specifically discloses the time expansion of an input signal by a factor of two and the corresponding time compression of an output signal in a manner inverse to that of the time expansion. Further, Awamoto uses two video heads mounted on a rotary drum "of any {*1533} of a well known video tape loading mechanism such that [the heads] follow parallel tracks skewed relative to the length of video tape." Driessen discloses a recording systemusing two pairs of heads mounted on piezoceramic actuators.

- - -Footnotes- - -

n1 The claims stand or fall together since no separate argument for patentability has been made for each claim.

- - -End Footnotes- - -

The Board concluded that the subject matter of the claims would have been obvious over Awamoto in view of Driessen, stating that "the time expansion or time compression relationship is satisfied for the expansion of two disclosed [in] Awamoto when a wrapping {**6} angle of 360 degrees, one pair of heads and no non-recording intervals are assumed." The Board further asserted that the recognition of the claimed relationship between time expansion/compression and the three variables a, n, and M is "the mere discoveryof a relationship that is applicable to [a] prior art apparatus[, and] does not [give] rise to a patentable invention." Thus, in affirming the rejection, the Board first assumed that the claim limitation at issue, the relationship between time expansion/compression and the three variables, was somehow "inherent" in the prior art as shown by Awamoto. The Board also assumed specific values for the claimed variables in order to assert that Awamoto's device satisfies the claimed relationship.

Rijckaert argues that the examiner has not established a prima faciecase of obviousness and that the examiner's assumptions do not constitute the disclosure of prior art. We agree. Awamoto does not disclose the wrapping angle of the record carrier around the head drum or the number of times that a head pair which comes in contact with the record carrier does not record a signal on the record carrier. Nor does Awamoto discuss the claimed relationship {**7} of the three variables to time expansion/compression. n2 Driessen, the secondary reference, is relied upon only to teach the provision of a pair of write heads having a mechanically rigid coupling to each other and does not remedy the deficiencies of Awamoto. Thus, the prior art relied upon does notdisclose, suggest, or render obvious the claimed invention, either individually or when combined. n3

- - -Footnotes- - -

n2 The Commissioner admits that other limitations recitedin claims 11 and 12 are not found in Awamoto; however, those limitations were not argued before the Board or this court. Thus, we agree with the Commissioner that those limitations are not at issue here.

n3 The Board also noted that the claims are not "specific" in that they claim the three variables as a "factor" of the expansion or compression time. The Board stated, "claims 11 and 12 fail to say which of expansion time or compression time is factored by the variables, how or when one of the two times is selected based on the variables or how each of the two times is related to the variables." The Board further stated, "the relationship is probably satisfied by any prior art video tape recording and reproducing apparatus that otherwise satisfies the remaining requirements of the claims at bar." While the Board's position implies a possible rejection based upon **35 U.S.C. §112,**this issue is not before us. In any event, the statement that the relationship is "probably satisfied" by the priorart is speculative and therefore does not establish a prima faciecase of unpatentability.

- - -End Footnotes- - -

{**8}

Awamoto does not describe the use of time expansion and compression as a means of optimally filling tracks, much less suggest that the three variables of the claims are even a factor in determining the amount of time expansion or time compression. Rather, Awamoto is concerned primarily with processing a high-quality broadcast television signal for use in conventional video machinery, and with compensating for errors introduced to such a signal by a transfer circuit. The Commissioner's assertion "that the [analysis discussed in his brief] and Awamoto demonstrate that the relationship was, in fact, well known in the art" is unavailing. While the court appreciates the Commissioner's thorough explanation of the claimed relationship in his brief, the Commissioner's brief is not prior art. The prior art is Awamoto, and it does not indicate that the relationship iswell known in the art, nor does it suggest the claimed relationship. See **In re Yates, 663 F.2d 1054, 211 USPQ 1149, 1151 (CCPA 1981)**(when the PTO asserts that there is an explicit or implicit teaching or suggestion in the prior art, it must indicate where such a teaching or suggestion {**9} appears inthe reference).

To support the Board's affirmance of the rejection,the Commissioner points out that in the recording art, the exact matching of signal time to recording time is an optimal {*1534} condition, and that this condition wouldbe met by fulfilling the claimed relationship. While the condition described may be an optimal one, it is not "inherent" in Awamoto. Nor are the means to achieve this optimal condition disclosed by Awamoto, explicitly or implicitly. "The mere fact that a certain thing mayresult from a given set of circumstances is not sufficient [to establish inherency.]" **In re Oelrich, 666 F.2d 578, 581-82, 212 USPQ 323, 326 (CCPA 1981)**(citations omitted) (emphasis added). "That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown." **In re Spormann, 53 C.C.P.A. 1375, 363 F.2d 444, 448, 150 USPQ 449, 452 (CCPA 1966).**Such a retrospective view of inherency is not a substitute for some teaching or suggestion supporting an obviousness rejection. See **In re Newell, 891 F.2d 899, 901, 13 USPQ2d 1248, 1250 (Fed. Cir. 1989).**{**10}

Rijckaert also argues that the rejection of dependent claim 6 as being obvious over Awamoto and Driessen in view of Ohta is improper. Ohta discloses an apparatus for compensating for signal loss in a single-head video recorder usinga time compression factor of 3/5 (a signal of time period5t/4 is compressed into a track of time period 3t/4) so that a signal is recorded completely during the time periodthat it takes the recording head to scan the magnetic tape. Regarding the Ohta patent, the examiner stated, "Ohta was only relied upon to support the idea that other compression factors are used in the prior art . . . ." n4 The relationship between the time expansion/compression and the three variables recited in the claims from which claim 6 depends, which is absent in the combination of Awamoto and Driessen, is not supplied by Ohta. Thus, we agree that the rejection of claim 6 under §103 is improper for the reasons set forth above with respect to the other claims.

- - -Footnotes- - -

n4 The Board did not specifically address the rejection of claim 6; therefore, claim 6 was considered to be affirmed for the reasons stated by the examiner. See**37 C.F.R. §1.196(a)**(1993).

- - -End Footnotes- - -

{**11}

While the Commissioner criticizes Rijckaert's arguments regarding the §103 rejections, the burden to rebut a rejection of obviousness does not arise until a prima faciecase has been established. In the case before us, it was not.

CONCLUSION

The decision of the United States Patent and Trademark Office Board of Patent Appeals and Interferences affirming the final rejection is reversed.

REVERSED

IN RE ANTHONY J. ROBERTSON and CHARLES L. SCRIPPS

98-1270

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

169 F.3d 743; 1999 U.S. App. LEXIS 3224; 49 U.S.P.Q.2D (BNA) 1949

February 25, 1999, Decided

PRIOR HISTORY:{**1} Appealed from: Patent and Trademark Office Board of Patent Appeals and Interferences. (Serial No. 08/171,484).

DISPOSITION:REVERSED.

COUNSEL: Kenneth R. Adamo, Jones, Day, Reavis &Pogue, of Cleveland, Ohio, argued for appellant. With himon the brief were Calvin P. Griffith, and Gregory A. Castanias, of Washington, DC. Of counsel on the brief was Steven W. Miller, The Proctor &Gamble Company, of Cincinnati, Ohio.

Linda Moncys Isacson, Associate Solicitor, Office of the Solicitor, of Arlington, Virginia, argued for appellee. With her on the brief were Albin F. Drost, Acting Solicitor, and John M. Whealan, Associate Solicitor.

JUDGES: Before NEWMAN, Circuit Judge, FRIEDMAN, Senior Circuit Judge, and RADER, Circuit Judge. Opinion for the court filedby Senior Circuit Judge FRIEDMAN, in which Circuit Judge NEWMAN joins. Concurring opinion filed by Circuit Judge RADER.

OPINIONBY:FRIEDMAN

OPINION:

{*744} FRIEDMAN, Senior Circuit Judge:

This appeal challenges the decision of the Board of PatentAppeals and Interferences (Board) that claim 76 in the appellants' patent application was anticipated by and obvious over United States Patent No. **4,895,569**(the Wilson patent). We reverse.

I

Both claim 76 and {**2} Wilson involve fastening and disposal systems for diapers. In both, the body of the diaper features a small front and a larger rear section. The outer edges of those sections are attached at the wearer's waist in the hip area. Once the diaper is soiled and then removed, the smaller front section is rolled up into the larger rear section and secured in this rolled-up configuration by fasteners.

The appellants' application is for "an improved mechanicalfastening system for . . . disposable absorbent articles [i.e., diapers] that provides convenient disposal of the absorbent article." Claim 76 covers:

> [A] mechanical fastening system for forming side closures . . . comprising a closure member . . . comprising a first mechanical fastening means for forming a closure, said first mechanical fastening means comprising a first fastening element; a landing member . . . comprising a second mechanical fastening means for forming a closure with said first mechanical fastening means, said second mechanical fastening means comprising a second fastening element mechanically engageable with said first element; and disposal means for allowing the absorbent article {**3} to be secured in a disposal configuration after use, said disposal means comprising a third mechanical fastening means for securing the absorbent article in the disposal configuration, said third mechanical fastening means comprising a third fastening element mechanically engageable with said first fastening element . . .

Claim 76 thus provides for two mechanical fastening means to attach the diaper to the wearer and a third such means for securing the diaper for disposal.

The Wilson patent discloses two snap elements on fasteningstrips attached to the outer edges of the front and rear hip sections of the garment. The fastening strips may alsoinclude "secondary load-bearing closure means" - additional fasteners to secure the garment; they may be identical to the snaps.

Wilson also states:

> Disposal of the soiled garment upon removal from the body is easily accomplished by folding the front panel .. . inwardly and then fastening the rear pair of mating fastener members . . . to one another, thus

> neatly bundlingthe garment into a closed compact package for disposal.

{*745} In other words, Wilson does not provide a separate fastening means to be used in disposing of the {**4}diaper. Instead, it suggests that disposal of the used diaper may be "easily accomplished" by rolling it up and employing the same fasteners used to attach the diaper to the wearer to form "a closed compact package for disposal."

In holding that the invention claim 76 covers was anticipated by Wilson, the Board did not hold that Wilson set forth a third fastening means. Instead, it found that Wilson anticipated claim 76 "under principles of inherency." Applying the language of claim 76 to the operation of Wilson, it concluded that "an artisan would readily understand the disposable absorbent garment of Wilson . . . as being inherently capable of [making the secondary load-bearing closure means] (third fastening element) mechanically engageable with [the other snap fasteners on the fastening strip] (first fastening element)" - i.e., using the secondary closure not with its mate, but with one of the primary snap fasteners. The Board summarily affirmed the examiner's alternative ruling that claim 76 would have been obvious in light of Wilson because "claim 76 lacks novelty."

II

Anticipation under **35 U.S.C. §102**(e) requires that "each and every element as set forth in the {**5} claim is found, either expressly or inherently described, in a single prior art reference." **Verdegaal Bros., Inc. v. Union Oil Co., 814 F.2d 628, 631, 2 U.S.P.Q.2D (BNA) 1051, 1053 (Fed. Cir. 1987).**

A. The Wilson patent does not expressly include a third fastening means for disposal of the diaper, as claim 76 requires. That means is separate from and in addition to the other mechanical fastening means and performs a different function than they do. Indeed, Wilson merely suggests that the diaper may be closed for disposal by using the same fastening means that are used for initially attaching the diaper to the body.

B. If the prior art reference does not expressly set fortha particular element of the claim, that reference still may anticipate if that element is "inherent" in its disclosure. To establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." **Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268, 20 U.S.P.Q.2D (BNA) 1746, 1749 (Fed. Cir. 1991).**"Inherency, however, may not be established by probabilities or {**6} possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." **Id. at 1269, 20 U.S.P.Q.2D (BNA) at 1749**(quoting **In re Oelrich, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981).**

In finding anticipation by inherency, the Board ignored the foregoing critical principles. The Board made no attemptto show that the fastening mechanisms of Wilson that wereused to attach the diaper to the wearer also "necessarily" disclosed the third separate fastening mechanism of claim 76 used to close the diaper for disposal, or that an artisan of ordinary skill would so recognize. It cited no extrinsic evidence so indicating.

Instead, the Board ruled that one of the fastening means for attaching the diaper to the wearer also could operate as a third fastening means to close the diaper for disposaland that Wilson therefore inherently contained all the elements of claim 76. In doing so, the Board failed to recognize that the third mechanical fastening means in claim 76, used to secure the diaper for disposal, was separate from and independent of the two other mechanical means used to attach the diaper to the person. The Board's theory that{**7} these two fastening devices in Wilson were capable of being intermingled to perform the same function as the third and first fastening elements in claim 76 is insufficient to show that the latter device was inherent in Wilson. Indeed, the Board's analysis rests upon the very kindof probability or possibility - the odd use of fasteners with other than their mates - that this court has pointed out is insufficient to establish inherency.

III

The Board's entire discussion of obviousness was as follows:

> {*746} **The rejection of claim 76 under 35 USC §103** We sustain the rejection of claim 76 under **35 USC §103.** Above, we found that claim 76 lacks novelty. Lack of novelty is the ultimate of obviousness. See **In re Fracalossi, 681 F.2d 792, 794, 215 U.S.P.Q. (BNA) 569, 571 (CCPA 1982).**Thus, claim 76 is appropriately rejected under **35 USC §103**as being unpatentable.

The "lack of novelty" upon which the Board based its conclusion of obviousness, however, was its finding of anticipation. Our rejection of that finding eliminates the sole basis of the Board's obviousness determination, which therefore cannot stand. See **In re Adams, 53 C.C.P.A. 1433, 364 F.2d 473, 480, 150 U.S.P.Q. 646, {**8} 651 (C.C.P.A. 1966).**

In his brief the Commissioner argues:

> Moreover, even if this court interprets claim 76 torequire two separate fasteners to perform the closure anddisposal func-

> tions, it would have been well within the knowledge of one of ordinary skill in the art to take Wilson's one fastener and make it into two separate fasteners. See[**In re] Graves, 69 F.3d [1147,] 1152, 36 U.S.P.Q.2D (BNA) [1697,] 1701**[(Fed. Cir. 1995)] (When evaluating a reference, it is appropriate to consider the knowledge of a skilled artisan in combination with the teaching of the reference.). Accordingly, claim 76 would have been obvious to one of ordinaryskill in the art, and the rejection should be affirmed bythis Court.

That, of course, was not the ground on which the Board based its obviousness ruling. We decline to consider counsel's newly-minted theory as an alternative ground for upholding the agency's decision. See **In re Soni, 54 F.3d 746, 751, 34 U.S.P.Q.2D (BNA) 1684, 1688 (Fed. Cir. 1995)**(citing **In re DeBlauwe, 736 F.2d 699, 705 n.7, 222 U.S.P.Q. 191, 196 n.7 (Fed. Cir. 1984)**.The Board's obviousness ruling cannot be sustained on theground the Board gave. {**9}

CONCLUSION

The decision of the Board of Patent Appeals and Interferences affirming the examiner's rejection of claim 76 as anticipated by and obvious over the Wilson patent is

REVERSED.

CONCURBY:RADER

CONCUR:
RADER, Circuit Judge, concurring.

Robertson asserts that the prior art Wilson patent does not teach three elements of claim 76: a "third mechanical fastening means," a disposal means on the "outside surface" of the body portion, and end regions that are "in an overlapping configuration when worn." In reversing the Board, this court relies solely on the purported failure of Wilsonto teach the third fastening means. Because I believe Wilson teaches such a means, but does not teach the other twolimitations at issue, I concur.

In its analysis, this court assumes without discussion that the claimed "third mechanical fastening means" covers a separatethird mechanical fastening means. This issue is key, for if the claim does not require a separate third fastening means, but instead allows the first fastening means to alsoserve as the third, then the prior art Wilson patent clearly teaches that element of the claim. For two reasons, this claim does not, to my eyes, {**10} require a separate third fastening means. First, the claim does not specifically recite a separatethird fastening means. Second, because the claim is in means-plus-function form, this court consults the specification to identify structure. The specification explicitly teaches that the first and third fastening elements can be the same so long as they are complementary, as they are in Wilson. Accordingly, I agree with the Board that Wilson teaches the claimed "third fastening element."

Wilson does not, however, teach either of the other two claim limitations at issue. As to the disposal means on the "outside surface" of the body portion, Wilson's figs. 12 and 13a-d show the disposal means on the inside of the bodyportion. As to the end regions that are "in an overlapping configuration when worn," Wilson explicitly teaches thatthe end regions should abut, not overlap, when worn. To overcome these teachings, the Board relied on the followingstatement in Wilson: "Further, the fastener members {*747} need not be previously mounted on a separate strip as shown then bonded . . . to the stretchable outer cover .. . . Multi-component snaps are available which may be applied directly to a {**11} stretchable outer cover material . . . ." Col. 7, l. 65 to col. 8, l. 3. The Board opined that applying snaps directly to the outer cover would result in both a disposal means on the "outside surface" and end regions "in an overlapping configuration when worn." Simply put, the Board has put more weight on this teaching than it can bear. It is far from clear what effect applying the snaps directly to the outer cover will have on the Wilson diaper configuration, let alone that it will result in a configuration satisfying the claim elements at issue. Accordingly, because I believe that the Board clearly erred in this interpretation of Wilson, I would reverse onthis ground.

ant as well as the public interest, the Commission abuses its discretion by declining to release the bond merely because of sales by a respondent of goods known to the complainant at the time of the agreement.

Biocraft also makes other arguments which we need not address.

CONCLUSION

The Commission's denials of Biocraft's requests for return or cancellation of bonds posted pursuant to the Temporary Cease and Desist Order issued January 10, 1990, were an abuse of discretion. Its order is therefore

REVERSED.

In re Mark A. VAECK, Wipa Chungjatupornchai and Lee McIntosh.

No. 91-1120.

United States Court of Appeals, Federal Circuit.

Oct. 21, 1991.

Inventor sought patent for claimed invention directed to use of genetic engineering techniques for production of insecticidal proteins. The United States Patent and Trademark Office Board of Patent Appeals and Interferences affirmed an examiner's rejection of certain claims, and appeal was taken. The Court of Appeals, Rich, Circuit Judge, held that: (1) patent application was improperly rejected on ground of prima facie obviousness, and (2) patent application was properly rejected to extent that claims were too general to enable person skilled in art to make and use claimed invention without undue experimentation.

Affirmed in part, reversed in part.

Mayer, Circuit Judge, dissented and filed opinion.

1. Patents ⇐314(5)

Obviousness of invention for which patent is sought is legal question which court independently reviews, though based upon Patent and Trademark Office's underlying factual findings, which court reviews under clearly erroneous standard. 35 U.S.C.A. § 103.

2. Patents ⇐16(2)

In reviewing rejection of invention for patent as obvious in view of combination of prior art references, court considers whether prior art would have suggested to those of ordinary skill in art that they should make claimed composition or device, or carry out claimed process, and whether prior art would also have revealed that in so making or carrying out, those of ordinary skill would have reasonable expectation of success; both suggestion and reasonable expectation of success must be found in prior art, not in applicant's disclosure. 35 U.S.C.A. § 103.

3. Patents ⇐16.25

Patent application for genetic engineering techniques for production of insecticidal proteins was improperly rejected on ground of prima facie obviousness; prior art did not disclose or suggest expression in cyanobacteria of chimeric gene encoding insecticidally active protein, or convey to those of ordinary skill reasonable expectation of success in doing so. 35 U.S.C.A. § 103.

4. Patents ⇐99

To be patentable, specification of patent must enable any person skilled in art to which it pertains to make and use claimed invention without undue experimentation. 35 U.S.C.A. § 112.

5. Patents ⇐99

Patent application for using genetic engineering techniques to produce insecticidal proteins was properly rejected to extent that claims were too general to enable person skilled in art to make and use claimed invention without undue experimentation; claim referred to use of cyanobacteria in general as host organism, despite fact that cyanobacteria were diverse and relatively poorly studied group of organisms, comprising some 150 different genera, with successful use of any one type in manner called for in invention being unpredictable. 35 U.S.C.A. § 112.

6. Patents ⇐99

Although patent applicants are not required to disclose every species encompassed by their claims, even in unpredictable art, in order to satisfy enablement requirement for patentability, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use invention as broadly as it is claimed. 35 U.S.C.A. § 112.

Ian C. McLeod, Ian C. McLeod, P.C., Okemos, Mich., argued for appellant.

Teddy S. Gron, Associate Sol., Office of the Sol., of Arlington, Va., argued for appellee. With him on the brief were Fred E. McKelvey, Sol. and Richard E. Schafer, Associate Sol.

Before RICH, ARCHER, and MAYER, Circuit Judges.

RICH, Circuit Judge.

This appeal is from the September 12, 1990 decision of the Patent and Trademark Office (PTO) Board of Patent Appeals and Interferences (Board), affirming the examiner's rejection of claims 1–48 and 50–52 of application Serial No. 07/021,405, filed March 4, 1987, titled "Hybrid Genes Incorporating a DNA Fragment Containing a Gene Coding for an Insecticidal Protein, Plasmids, Transformed Cyanobacteria Expressing Such Protein and Method for Use as a Biocontrol Agent" as unpatentable under 35 U.S.C. § 103, as well as the rejection of claims 1–48 and 50–51 under 35 U.S.C. § 112, first paragraph, for lack of enablement. We reverse the § 103 rejection. The § 112 rejection is affirmed in part and reversed in part.

1. Basic vocabulary and techniques for gene cloning and expression have been described in *In re O'Farrell*, 853 F.2d 894, 895–99, 7 U.S.P.Q.2d 1673, 1674–77 (Fed.Cir.1988), and are not repeated here.

2. All living cells can be classified into one of two broad groups, procaryotes and eucaryotes. The procaryotes comprise organisms formed of cells that do not have a distinct nucleus; their DNA floats throughout the cellular cytoplasm. In contrast, the cells of eucaryotic organisms such as man, other animals, plants, protozoa, algae and yeast have a distinct nucleus wherein their DNA resides.

BACKGROUND

A. The Invention

The claimed invention is directed to the use of genetic engineering techniques [1] for production of proteins that are toxic to insects such as larvae of mosquitos and black flies. These swamp-dwelling pests are the source of numerous human health problems, including malaria. It is known that certain species of the naturally-occurring *Bacillus* genus of bacteria produce proteins ("endotoxins") that are toxic to these insects. Prior art methods of combatting the insects involved spreading or spraying crystalline spores of the insecticidal *Bacillus* proteins over swamps. The spores were environmentally unstable, however, and would often sink to the bottom of a swamp before being consumed, thus rendering this method prohibitively expensive. Hence the need for a lower-cost method of producing the insecticidal *Bacillus* proteins in high volume, with application in a more stable vehicle.

As described by appellants, the claimed subject matter meets this need by providing for the production of the insecticidal *Bacillus* proteins within host cyanobacteria. Although both cyanobacteria and bacteria are members of the procaryote [2] kingdom, the cyanobacteria (which in the past have been referred to as "blue-green algae") are unique among procaryotes in that the cyanobacteria are capable of oxygenic photosynthesis. The cyanobacteria grow on top of swamps where they are consumed by mosquitos and black flies. Thus, when *Bacillus* proteins are produced with-

in transformed[3] cyanobacterial hosts according to the claimed invention, the presence of the insecticide in the food of the targeted insects advantageously guarantees direct uptake by the insects.

More particularly, the subject matter of the application on appeal includes a chimeric (i.e., hybrid) gene comprising (1) a gene derived from a bacterium of the *Bacillus* genus whose product is an insecticidal protein, united with (2) a DNA promoter effective for expressing[4] the *Bacillus* gene in a host cyanobacterium, so as to produce the desired insecticidal protein.

The claims on appeal are 1–48 and 50–52, all claims remaining in the application. Claim 1 reads:

> 1. A chimeric gene capable of being expressed in Cyanobacteria cells comprising:
>
> (a) a DNA fragment comprising a promoter region which is effective for expression of a DNA fragment in a Cyanobacterium; and
>
> (b) at least one DNA fragment coding for an insecticidally active protein produced by a Bacillus strain, or coding for an insecticidally active truncated form of the above protein or coding for a protein having substantial sequence homology to the active protein,
>
> the DNA fragments being linked so that the gene is expressed.

Claims 2–15, which depend from claim 1, recite preferred *Bacillus* species, promoters, and selectable markers.[5] Independent claim 16 and claims 17–31 which depend therefrom are directed to a hybrid plasmid vector which includes the chimeric gene of claim 1. Claim 32 recites a bacterial strain. Independent claim 33 and claims 34–48 which depend therefrom recite a cyanobacterium which expresses the chimeric gene of claim 1. Claims 50–51 recite an insecticidal composition. Claim 52 recites a particular plasmid that appellants have deposited.

B. *Appellants' Disclosure*

In addition to describing the claimed invention in generic terms, appellants' specification discloses two particular species of *Bacillus* (*B. thuringiensis, B. sphaericus*) as sources of insecticidal protein; and nine genera of cyanobacteria (*Synechocystis, Anacystis, Synechococcus, Agmenellum, Aphanocapsa, Gloecapsa, Nostoc, Anabaena* and *Ffremyllia*) as useful hosts.

The working examples relevant to the claims on appeal detail the transformation of a single strain of cyanobacteria, i.e., *Synechocystis* 6803. In one example, *Synechocystis* 6803 cells are transformed with a plasmid comprising (1) a gene encoding a particular insecticidal protein ("B.t. 8") from *Bacillus thuringiensis* var. *israelensis*, linked to (2) a particular promoter, the P_L promoter from the bacteriophage Lambda (a virus of *E. coli*). In another example, a different promoter, i.e., the *Synechocystis* 6803 promoter for the rubisco operon, is utilized instead of the Lambda P_L promoter.

C. *The Prior Art*

A total of eleven prior art references were cited and applied, in various combinations, against the claims on appeal.

The focus of Dzelzkalns,[6] the primary reference cited against all of the rejected claims, is to determine whether chloroplast promoter sequences can function in cyanobacteria. To that end Dzelzkalns discloses the expression in cyanobacteria of a chimeric gene comprising a chloroplast promoter sequence fused to a gene encoding the enzyme chloramphenicol acetyl transferase (CAT).[7] Importantly, Dzelzkalns teaches the use of the CAT gene as a "marker" gene; this use of antibiotic resistance-conferring genes for selection purposes is a common technique in genetic engineering.

Sekar I,[8] Sekar II,[9] and Ganesan[10] collectively disclose expression of genes encoding certain *Bacillus* insecticidal proteins in the bacterial hosts *B. megaterium, B. subtilis* and *E. coli*.

Friedberg[11] discloses the transformation of the cyanobacterium *Anacystis nidulans* R2 by a plasmid vector comprising the O_LP_L operator-promoter region and a temperature-sensitive repressor gene of the bacteriophage Lambda. While the cyanobacteria are attractive organisms for the cloning of genes involved in photosynthesis, Friedberg states, problems may still be encountered such as suboptimal expression of the cloned gene, detrimental effects on cell growth of overexpressed, highly hydrophobic proteins, and rapid turnover of some gene products. To address these problems, Friedberg teaches the use of the disclosed Lambda regulatory signals in plasmid vehicles which, it states, have "considerable potential for use as vectors the expression of which can be controlled in *Anacystis*...."

Miller[12] compares the initiation specificities *in vitro* of DNA-dependent RNA polymerases[13] purified from two different species of cyanobacteria (*Fremyella diplosiphon* and *Anacystis nidulans*), as well as from *E. coli*.

Nierzwicki-Bauer[14] identifies in the cyanobacterium *Anabaena* 7120 the start site for transcription of the gene encoding *rbcL*, the large subunit of the enzyme ribulose–1,5–bisphosphate carboxylase. It reports that the nucleotide sequence 14–8 base pairs preceding the transcription start site "resembles a good *Escherichia coli* promoter," but that the sequence 35 base pairs before the start site does not.

Chauvat[15] discloses host-vector systems for gene cloning in the cyanobacterium *Synechocystis* 6803, in which the antibiotic resistance-conferring *neo* gene is utilized as a selectable marker.

Reiss[16] studies expression in *E. coli* of various proteins formed by fusion of certain foreign DNA sequences with the *neo* gene.

Kolowsky[17] discloses chimeric plasmids designed for transformation of the cyanobacterium *Synechococcus* R2, comprising an antibiotic-resistant gene linked to chromosomal DNA from the *Synechococcus* cyanobacterium.

Barnes, United States Patent No. 4,695,455, is directed to the treatment with stabilizing chemical reagents of pesticides produced by expression of heterologous genes (such as those encoding *Bacillus* proteins) in host microbial cells such as *Pseudomonas* bacteria. The host cells are killed by this treatment, but the resulting pesticidal compositions exhibit prolonged toxic activity when exposed to the environment of target pests.

3. "Transformed" cyanobacteria are those that have successfully taken up the foreign *Bacillus* DNA such that the DNA information has become a permanent part of the host cyanobacteria, to be replicated as new cyanobacteria are generated.

4. "Expression" of a gene refers to the production of the protein which the gene encodes; more specifically, it is the process of transferring information from a gene (which consists of DNA) via messenger RNA to ribosomes where a specific protein is made.

5. In the context of the claimed invention, "selectable markers" or "marker genes" refer to antibiotic-resistance conferring DNA fragments, attached to the gene being expressed, which facilitate the selection of successfully transformed cyanobacteria.

6. 12 *Nucleic Acids Res.* 8917 (1984).

7. Chloramphenicol is an antibiotic; CAT is an enzyme which destroys chloramphenicol and thus imparts resistance thereto.

8. 137 *Biochem. and Biophys. Res. Comm.* 748 (1986).

9. 33 *Gene* 151 (1985).

10. 189 *Mol. Gen. Genet.* 181 (1983).

11. 203 *Mol. Gen. Genet.* 505 (1986).

12. 140 *J. Bacteriology* 246 (1979).

13. RNA polymerase, the enzyme responsible for making RNA from DNA, binds at specific nucleotide sequences (promoters) in front of genes in DNA, and then moves through the gene making an RNA molecule that includes the information contained in the gene. Initiation specificity is the ability of the RNA polymerase to initiate this process specifically at a site(s) on the DNA template.

14. 81 *Proc. Natl. Acad. Sci. USA* 5961 (1984).

15. 204 *Mol. Gen. Genet.* 185 (1986).

16. 30 *Gene* 211 (1984).

17. 27 *Gene* 289 (1984).

D. The Grounds of Rejection

1. The § 103 Rejections

Claims 1–6, 16–21, 33–38, 47–48 and 52 (which include all independent claims in the application) were rejected as unpatentable under 35 U.S.C. § 103 based upon Dzelzkalns in view of Sekar I or Sekar II and Ganesan. The examiner stated that Dzelzkalns discloses a chimeric gene capable of being highly expressed in a cyanobacterium, said gene comprising a promoter region effective for expression in a cyanobacterium operably linked to a structural gene encoding CAT. The examiner acknowledged that the chimeric gene and transformed host of Dzelzkalns differ from the claimed invention in that the former's structural gene encodes CAT rather than insecticidally active protein. However, the examiner pointed out, Sekar I, Sekar II, and Ganesan teach genes encoding insecticidally active proteins produced by *Bacillus*, and the advantages of expressing such genes in heterologous [18] hosts to obtain larger quantities of the protein. The examiner contended that it would have been obvious to one of ordinary skill in the art to substitute the *Bacillus* genes taught by Sekar I, Sekar II, and Ganesan for the CAT gene in the vectors of Dzelzkalns in order to obtain high level expression of the *Bacillus* genes in the transformed cyanobacteria. The examiner further contended that it would have been obvious to use cyanobacteria as heterologous hosts for expression of the claimed genes due to the ability of cyanobacteria to serve as transformed hosts for the expression of heterologous genes. In the absence of evidence to the contrary, the examiner contended, the invention as a whole was prima facie obvious.

Additional rejections were entered against various groups of dependent claims which we need not address here. All additional rejections were made in view of Dzelzkalns in combination with Sekar I, Sekar II, and Ganesan, and further in view of other references discussed in Part C above.

The Board affirmed the § 103 rejections, basically adopting the examiner's Answer as its opinion while adding a few comments. The legal conclusion of obviousness does not require absolute certainty, the Board added, but only a reasonable expectation of success, citing *In re O'Farrell*, 853 F.2d 894, 7 U.S.P.Q.2d 1673 (Fed. Cir.1988). In view of the disclosures of the prior art, the Board concluded, one of ordinary skill in the art would have been motivated by a reasonable expectation of success to make the substitution suggested by the examiner.

2. The § 112 Rejection

The examiner also rejected claims 1–48 and 50–51 under 35 U.S.C. § 112, first paragraph, on the ground that the disclosure was enabling only for claims limited in accordance with the specification as filed. Citing *Manual of Patent Examining Procedure* (MPEP) provisions 706.03(n) [19] and (z) [20] as support, the examiner took the position that undue experimentation would be required of the art worker to practice the claimed invention, in view of the unpredictability in the art, the breadth of the claims, the limited number of working examples and the limited guidance provided in the specification. With respect to unpredictability, the examiner stated that

> [t]he cyanobacteria comprise a large and diverse group of photosynthetic bacteria including large numbers of species in some 150 different genera including *Synechocystis, Anacystis, Synechococcus, Agmenellum, Nostoc, Anabaena,* etc. The molecular biology of these organisms has only recently become the subject of intensive investigation and this work is limited to a few genera. Therefore the level of unpredictability regarding heterologous gene expression in this large, diverse and relatively poorly studied group of procaryotes is high....

The Board affirmed, noting that "the limited guidance in the specification, considered in light of the relatively high degree of unpredictability in this particular art, would not have enabled one having ordinary skill in the art to practice the broad scope of the claimed invention without undue experimentation. *In re Fisher*, 427 F.2d 833, 166 U.S.P.Q. 18 (CCPA 1970)."

18. Denotes different species or organism.

19. MPEP 706.03(n), "Correspondence of Claim and Disclosure," provides in part:

> In chemical cases, a claim may be so broad as to not be supported by [the] disclosure, in which case it is rejected as unwarranted by the disclosure....

20. MPEP 706.03(z), "Undue Breadth," provides in part:

> [I]n applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Sol*, 1938 C.D. 723; 497 O.G. 546. This is because in arts such as chemistry it is not obvious from the disclosure of one species, what other species will work. *In re Dreshfield*, 1940 C.D. 351; 518 O.G. 255 gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." ...

OPINION

A. *Obviousness*

[1] We first address whether the PTO erred in rejecting the claims on appeal as prima facie obvious within the meaning of 35 U.S.C. § 103. Obviousness is a legal question which this court independently reviews, though based upon underlying factual findings which we review under the clearly erroneous standard. *In re Woodruff*, 919 F.2d 1575, 1577, 16 U.S.P.Q.2d 1934, 1935 (Fed.Cir.1990).

[2] Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, *inter alia*, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *See In re Dow Chemical Co.*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531 (Fed.Cir.1988). Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant's disclosure. *Id.*

[3] We agree with appellants that the PTO has not established the prima facie obviousness of the claimed subject matter. The prior art simply does not disclose or suggest the expression in cyanobacteria of a chimeric gene encoding an insecticidally active protein, or convey to those of ordinary skill a reasonable expectation of success in doing so. More particularly, there is no suggestion in Dzelzkalns, the primary reference cited against all claims, of substituting in the disclosed plasmid a structural gene encoding *Bacillus* insecticidal proteins for the CAT gene utilized for selection purposes. The expression of antibiotic resistance-conferring genes in cyanobacteria, without more, does not render obvious the expression of unrelated genes in cyanobacteria for unrelated purposes.

The PTO argues that the substitution of insecticidal *Bacillus* genes for CAT marker genes in cyanobacteria is suggested by the secondary references Sekar I, Sekar II, and Ganesan, which collectively disclose expression of genes encoding *Bacillus* insecticidal proteins in two species of host *Bacillus* bacteria (*B. megaterium* and *B. subtilis*) as well as in the bacterium *E. coli*. While these references disclose expression of *Bacillus* genes encoding insecticidal proteins in certain transformed *bacterial* hosts, nowhere do these references disclose or suggest expression of such genes in transformed *cyanobacterial* hosts.

To remedy this deficiency, the PTO emphasizes similarity between bacteria and cyanobacteria, namely, that these are both procaryotic organisms, and argues that this fact would suggest to those of ordinary skill the use of cyanobacteria as hosts for expression of the claimed chimeric genes. While it is true that bacteria and cyanobacteria are now both classified as procaryotes, that fact alone is not sufficient to motivate the art worker as the PTO con-

tends. As the PTO concedes, cyanobacteria and bacteria are not identical; they are classified as two separate divisions of the kingdom Procaryotae.[21] Moreover, it is only in recent years that the biology of cyanobacteria has been clarified, as evidenced by references in the prior art to "blue-green algae." Such evidence of recent uncertainty regarding the biology of cyanobacteria tends to rebut, rather than support, the PTO's position that one would consider the cyanobacteria effectively interchangeable with bacteria as hosts for expression of the claimed gene.

At oral argument the PTO referred to additional secondary references, not cited against any independent claim (i.e., Friedberg, Miller, and Nierzwicki-Bauer), which it contended disclose certain amino acid sequence homology between bacteria and cyanobacteria. The PTO argued that such homology is a further suggestion to one of ordinary skill to attempt the claimed invention. We disagree. As with the Dzelzkalns, Sekar I, Sekar II, and Ganesan references discussed above, none of these additional references disclose or suggest that cyanobacteria could serve as hosts for expression of genes encoding *Bacillus* insecticidal proteins. In fact, these additional references suggest as much about *differences* between cyanobacteria and bacteria as they do about similarities. For example, Nierzwicki-Bauer reports that a certain nucleotide sequence (i.e., the -10 consensus sequence) in a particular cyanobacterium resembles an *E. coli* promoter, but that another nearby nucleotide sequence (the -35 region) does not. While Miller speaks of certain promoters of the bacteriophage Lambda that are recognized by both cyanobacterial and *E. coli* RNA polymerases, it also discloses that these promoters exhibited differing strengths when exposed to the different polymerases. Differing sensitivities of the respective polymerases to an inhibitor are also disclosed, suggesting differences in the structures of the initiation complexes.

The PTO asks us to agree that the prior art would lead those of ordinary skill to conclude that cyanobacteria are attractive hosts for expression of any and all heterologous genes. Again, we can not. The relevant prior art does indicate that cyanobacteria are attractive hosts for expression of both native and heterologous *genes involved in photosynthesis* (not surprisingly, for the capability of undergoing oxygenic photosynthesis is what makes the cyanobacteria unique among procaryotes). However, these references do not suggest that cyanobacteria would be equally attractive hosts for expression of *unrelated* heterologous genes, such as the claimed genes encoding *Bacillus* insecticidal proteins.

In *O'Farrell*, this court affirmed an obviousness rejection of a claim to a method for producing a "predetermined protein in a stable form" in a transformed bacterial host. 853 F.2d at 895, 7 U.S.P.Q.2d at 1674. The cited references included a prior art publication (the Polisky reference) whose three authors included two of the three coinventor-appellants. The main difference between the prior art and the claim at issue was that in Polisky, the heterologous gene was a gene for ribosomal RNA, while the claimed invention substituted a gene coding for a predetermined protein. *Id.* at 901, 7 U.S.P.Q.2d at 1679. Although, as the appellants therein pointed out, the ribosomal RNA gene is not normally translated into protein, Polisky mentioned preliminary evidence that the transcript of the ribosomal RNA gene was translated into protein, and further predicted that if a gene coding for a protein were to be substituted, extensive translation might result. *Id.* We thus affirmed, explaining that

> the prior art explicitly suggested the substitution that is the difference between the claimed invention and the prior art, and presented preliminary evidence suggesting that the [claimed] method could be used to make proteins.
>
> ....
>
> ... Polisky contained detailed enabling methodology for practicing the claimed invention, a suggestion to modify the prior art to practice the claimed invention, and evidence suggesting that it would be successful.

Id. at 901–02, 7 U.S.P.Q.2d at 1679–80.

In contrast with the situation in *O'Farrell*, the prior art in this case offers no suggestion, explicit or implicit, of the substitution that is the difference between the claimed invention and the prior art. Moreover, the "reasonable expectation of success" that was present in *O'Farrell* is not present here. Accordingly, we reverse the § 103 rejections.

B. Enablement

[4] The first paragraph of 35 U.S.C. § 112 requires, *inter alia*, that the specification of a patent enable any person skilled in the art to which it pertains to make and use the claimed invention. Although the statute does not say so, enablement requires that the specification teach those in the art to make and use the invention without "undue experimentation." *In re Wands*, 858 F.2d 731, 737, 8 U.S.P.Q.2d 1400, 1404 (Fed.Cir.1988). That *some* experimentation may be required is not fatal; the issue is whether the amount of experimentation required is "undue." *Id.* at 736–37, 8 U.S.P.Q.2d at 1404. Enablement, like obviousness, is a question of law which we independently review, although based upon underlying factual findings which we review for clear error. *See id.* at 735, 8 U.S.P.Q.2d at 1402.

[5] In response to the § 112 rejection, appellants assert that their invention is "pioneering," and that this should entitle them to claims of broad scope. Narrower claims would provide no real protection, appellants argue, because the level of skill in this art is so high, art workers could easily avoid the claims. Given the disclosure in their specification, appellants contend that any skilled microbiologist could construct vectors and transform many different cyanobacteria, using a variety of promoters and *Bacillus* DNA, and could easily determine whether or not the active *Bacillus* protein was successfully expressed by the cyanobacteria.

The PTO made no finding on whether the claimed invention is indeed "pioneering," and we need not address the issue here. With the exception of claims 47 and 48, the claims rejected under § 112 are not limited to any particular genus or species of cyanobacteria. The PTO's position is that the cyanobacteria are a diverse and relatively poorly studied group of organisms, comprising some 150 different genera, and that heterologous gene expression in cyanobacteria is "unpredictable." Appellants have not effectively disputed these assertions. Moreover, we note that only one particular species of cyanobacteria is employed in the working examples of appellants' specification, and only nine genera of cyanobacteria are mentioned in the entire document.

Taking into account the relatively incomplete understanding of the biology of cyanobacteria as of appellants' filing date, as well as the limited disclosure by appellants of particular cyanobacterial genera operative in the claimed invention, we are not persuaded that the PTO erred in rejecting claims 1–46 and 50–51 under § 112, first paragraph. There is no reasonable correlation between the narrow disclosure in appellants' specification and the broad scope of protection sought in the claims encompassing gene expression in any and all cyanobacteria. *See In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (CCPA 1970) (the first paragraph of § 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification).[22] Accordingly,

21. *Stedman's Medical Dictionary* 1139 (24th ed. 1982) (definition of "Procaryotae"). Procaryotic organisms are commonly classified according to the following taxonomic hierarchy: Kingdom; Division; Class; Order; Family; Genus; Species. 3 *Bergey's Manual of Systematic Bacteriology* 1601 (1989).

22. The enablement rejection in this case was not based upon a post-filing date state of the art, as in *In re Hogan*, 559 F.2d 595, 605–07, 194 U.S.P.Q. 527, 536–38 (CCPA 1977). *See also United States Steel Corp. v. Phillips Petroleum Co.*, 865 F.2d 1247, 1251, 9 U.S.P.Q.2d 1461, 1464 (Fed.Cir.1989) (citing *Hogan*); *Hormone Research Found., Inc. v. Genentech, Inc.*, 904 F.2d 1558, 1568–69, 15 U.S.P.Q.2d 1039, 1047–48 (Fed.Cir.1990) (directing district court, on remand, to consider effect of *Hogan* and *United States Steel* on the enablement analysis of *Fisher*), *cert. dismissed*, — U.S. —, 111 S.Ct. 1434, 113 L.Ed.2d 485 (1991). We therefore do not